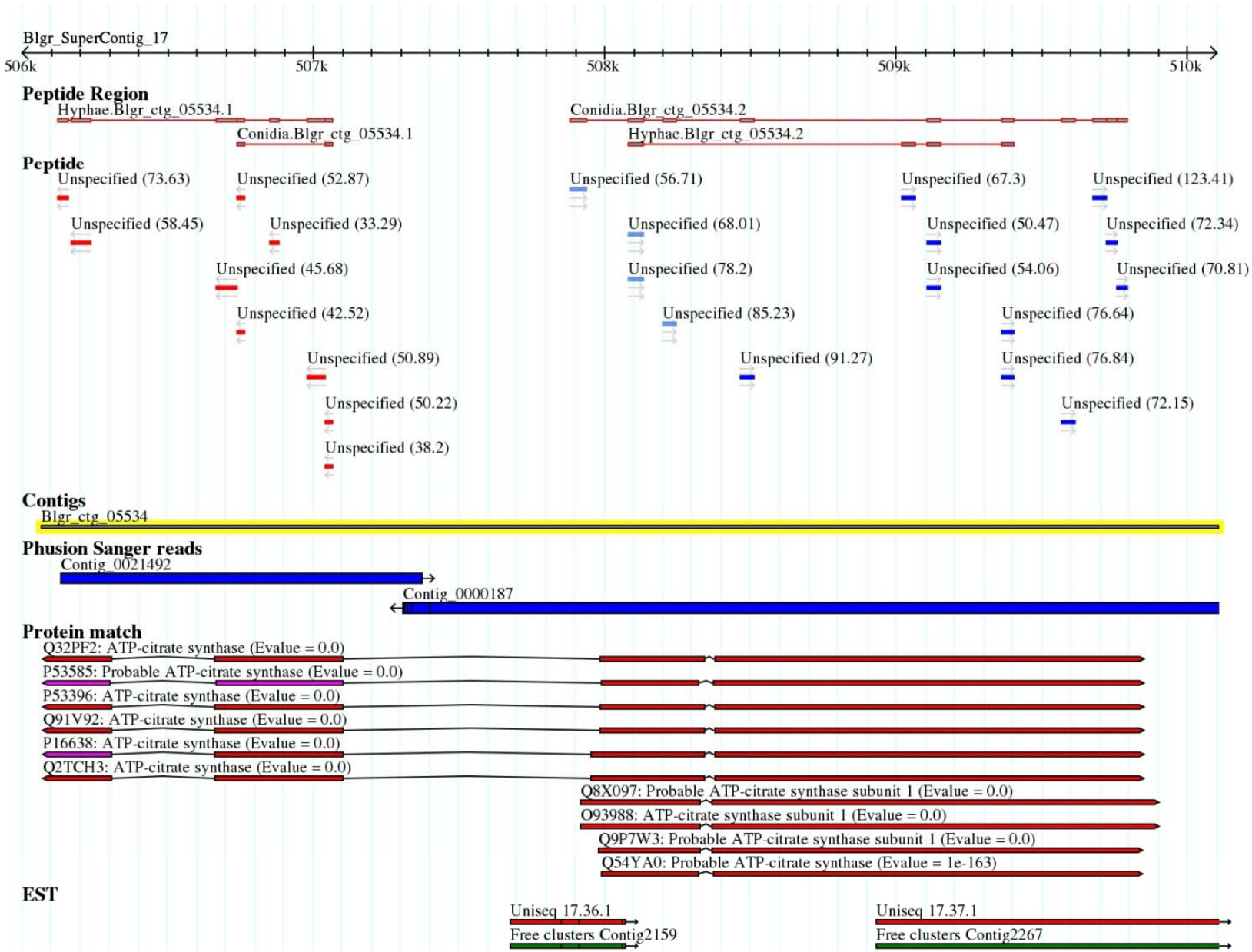Supplemental Data 2